UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES

Ex parte PETER T. PUGLIESE
(hereafter Pugliese)

Appeal No. 2005-0545
Application No. 09/989,019[1]

ON BRIEF

Before GRON, ADAMS and MILLS, Administrative Patent Judges.

GRON, Administrative Patent Judge.

DECISION ON APPEAL UNDER 35 U.S.C. § 134

Introduction

This is an appeal under 35 U.S.C. § 134 of an examiner's final rejection of claims pending in Application 09/989,019. All "oil-in-water emulsion" claims (Claims 1-7 and 9-11) stand twice rejected under 35 U.S.C. § 103 in view of the combined teachings of

[1] Application for patent filed November 21, 2001. Applicant claims benefit under 35 U.S.C. § 119(e) of the November 24, 2000, filing date of Provisional Application 60/250,397.

Soudant et al. (Soudant), U.S. 5,436,230, patented July 25, 1995; Koulbanis et al. (Koulbanis), U.S. 4,288,433, patented September 8, 1981; Majeed et al. (Majeed), U.S. 5,804,596, patented September 8, 1998; Sekiya, U.S. 5,776,906, patented July 7, 1998; De Simone et al. (De Simone), WO 98/01128, published January 15, 1998; Japanese Unexamined Patent Publication Hei 7-61927 (Lotte), published March 7, 1995;[2] Kuppusamy et al. (Kuppusamy), "Effects of Flavonoids on Cyclic AMP Phosphodiesterase and Lipid Mobilization in Rat Adipocytes," Biochemical Pharmacology, Vol. 44, No. 7, pp. 1307-1315 (1992); and Gennaro et al. (Gennaro), Remington's Pharmaceutical Sciences, 18th Ed., pp. 1305-1307 (1990). The status of Claim 8 is not entirely clear. In the Examiner's Answer, p. 2 (EA2), the examiner stated, "Upon reconsideration, claim 8, which [is] drawn to the method of treating cellulite, is allowed." Appellant's arguments were found "persuasive" (EA3). The examiner explained (EA3; emphasis added):

> Claim 8 directed to a method of treating cellulite is found allowable. Cited prior art, save Koulbanis and Soudant et al., are silent on treating cellulites. These anticellulites recitation [sic] are not regards [sic] to obviate the [sic] claims 1-7 and 9-11. Rebuttal arguments ar [sic, at] Brief, pages 8-12[,] are persuasive to support the use set forth in claim 8. [The] Examiner found the

[2] For purposes of this appeal, we refer to the English translation of Japanese Patent Document No. 07-061927 of record (PTO 03-2568 HAMT, pp. 1-14).

> presented arguments convincing and, thus, allowed claim 8. [The] Examiner notes that compositions of matter are useful for any purpose. Use not envisioned by Appellant can be applied to provide motivation for obviating composition claims.

To the extent we can decipher the examiner's unedited explanation for allowing Claim 8, we are confused at best. The examiner said (EA2), "The copy of the appealed claims contained in the Appendix to the brief is correct." See the Appendix to Appellant's Brief (AB). Accordingly, Claim 8 is directed to a "method of treating cellulitis in women wherein the application formulation comprises an oil-in water emulsion . . ." (emphasis added). On the other hand, Claim 1 is directed to an "oil-in-water emulsion suited for topical application to the skin of a woman evincing the cosmetic condition called cellulite . . ." (emphasis added). Having searched "allowed" Claim 8 for a single process step, we find none. Nevertheless, appellant argued a patentable distinction between treating the cosmetic condition called "cellulite" and treating the medical condition called "cellulitis" in his Brief (AB11-12; footnote included in main text):

> By way of example, Soudant, Majeed, Lotte, Sekiya, and De Simone are all directed to treatments for other human problems, like the varied manifestations of obesity. None, save Koulbanis, even speak to anti-cellulitis action. Cellulitis is inflammation of cellular or connective tissues, which is not CELLULITE, as defined herein. Taber's Medical Dictionary 1981 Ed. Pg. 37.

. . . . .

> Lastly, the enclosed Rule 132 Declaration establishes that representative flavones are capable of inhibiting the undesirable destructive effects of estrogen on connective tissue and thus provide a positive effect on treating cellulite, not cellulitis.

Contrary to appellant's view, yet consistent with statements of the examiner, we find that Koulbanis and Soudant both describe treatments for cellulitis. See Koulbanis, Abstract; col. 1, l. 7-9, 50, 56-57, 60, and 67-68; col. 2, l. 7-9; col. 3, l. 9-11; col. 4, l. 40, 54, 56, and 68; col. 5, l. 5, 54; and col. 6, l. 15 and 56. See Soudant, col. 1, l. 61-68; col. 2, l. 3-4; and col. 4, l. 58-64. Soudant defines "cellulitis" as "that swelling of the subcutaneous connective tissue . . . [which] gives the skin an 'upholstered' appearance" (Soudant, col. 1, l. 64-66). The condition defined as cellulitis is formed by local accumulation of fat and water trapped in a matrix of more or less fluid-tight compartments" (Soudant, col. 1, l. 66-68). Soudant would have taught persons having ordinary skill in the art that the condition known as cellulitis not only forms from, and is associated with, "local accumulation of fat" (Soudant, col. 1, l. 66-68), but also that one may treat associated cellulitis by treatments which combat local accumulation of fat. Soudant states (Soudant, col. 4, l. 58-64):

> A still further object of the present invention is a treatment method designed to combat cellulitis and local fat overload and to improve the aesthetic appearance of a person, characterized by the application to the skin or oral administration of a composition containing at least one . . . lipolytic active principle.

Soudant instructs (Soudant, col. 2, l. 3-7):

> Topical application of an anticellulitic agent may erase local accumulation of fat by lipolytic action. The best-known and most widespread method of stimulating lipolysis is by inhibiting phosphodiesterase to prevent or at least limit the rate of cyclic AMP breakdown.

Thus, absent evidence sufficient to establish that the invention of Claim 8 is patentably distinct from the invention of Claims 1-7 and 9-11, the patentability of the method of treating cellulitis of Claim 8 by topical application of a formulation of Claims 1-7 and 9-11 reasonably appears to stand or fall with the patentability of formulation Claims 1-7 and 9-11, stated as useful for topical application to the skin of a woman evincing the cosmetic condition called cellulite, in view of the combined prior art teachings. One or more of the applied prior art references teaches that at least one of the components of the rejected formulation is a phosphodiesterase inhibitor and is lipolytic. Thus, persons having ordinary skill in the art would reasonably have expected that such component could be topically applied to the skin to combat cellulitis. Soudant teaches compositions for topical treatment of cellulitis which may contain "lipolytic agents such as for example

xanthines, particularly caffeine, or . . . carnitine . . . (Soudant, col. 2, l. 29-34 (emphasis added)). The lipolytic agents stimulate lipolytic activity by inhibiting the action of phosphodiesterase (Soudant, col. 2, l. 3-24). Koulbanis also teaches topically applied compositions for treatment of cellulitis which contain xanthic bases such as theophylline, caffeine and theobromine which promote lipolysis activity by inhibiting phosphodiesterase activity (Koulbanis, col. 1, l. 34-50; col. 2, l. 56-62).

Discussion

The criterion for establishing a prima facie case of obviousness under 35 U.S.C. § 103 in view of combined prior art teachings "is not the number of references, but what they would have meant to a person of ordinary skill in the field of the invention." In re Gorman, 933 F.2d 982, 986, 18USPQ2d 1885, 1888 (Fed. Cir. 1991). Gorman instructs at 986, 18 USPQ2d at 1888:

> [W]hether a new combination of known elements would have been obvious to one of ordinary skill depends on various facts, including whether the elements exist in "analogous art", that is, art that is reasonably pertinent to the problem with which the inventor is concerned. . . . When the references are all in the same or analogous fields, knowledge thereof by the hypothetical person of ordinary skill is presumed . . . and the test is whether the teachings of the prior art, taken as a whole, would have made obvious the claimed invention.

However, Gorman cautioned, 933 F.2d at 986, 18USPQ2d at 1888:

> When it is necessary to select elements of various teachings in order to form the claimed invention, we ascertain whether there is any suggestion or motivation in the prior art to make the selection made by the applicant. . . . "'Obviousness can not be established by combining the teachings of the prior art to produce the claimed invention, absent some teaching, suggestion or incentive supporting the combination.'" In re Bond, 910 F.2d 831, 834, 15 USPQ2d 1566, 1568 (Fed. Cir. 1990) (quoting Carella v. Starlight Archery and Pro Line Co., 804 F.2d 135, 140, 231 USPQ 644, 647 (Fed. Cir. 1986).
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> The extent to which such suggestion must be explicit in, or may be fairly inferred from, the references, is decided on the facts of each case, in light of the prior art and its relationship to the applicant's invention. As in all determinations under 35 U.S.C. §103, the decision maker must bring judgment to bear. It is impermissible, however, simply to engage in a hindsight reconstruction of the claimed invention, using applicant's structure as a template and selecting elements from references to fill the gaps. . . . The references themselves must provide some teaching whereby the applicant's combination would have been obvious.

Accordingly, we first consider whether the combined prior art is reasonably pertinent to the problem with which the inventor is concerned, i.e., analogous "for the control and treatment of a cosmetic condition known as cellulite" (Specification (Spec.), p. 1, l. 8-9). Pugliese's "[t]reatment is directed at controlling the breakdown of collagen and reducing the fat mass to a smaller volume" (Spec., p. 1, l. 9-10). Pugliese recognizes that localized accumulation of fat is an important component of the condition called "cellulite" (Spec., p. 1, l. 12-17; emphasis added):

> [A] condition of the buttocks and upper thighs characterized by an unattractive, undulating, irregular skin surface. The condition has been thought by previous investigators to originate from abnormal fatty deposits that collected under the skin. Many attempts have been made to define cellulite but no adequate explanation has been forthcoming. While fat is not the major etiological factor in cellulite, it is an important component of the condition.

Pugliese teaches that "[t]he use agents that are capable of lipolytic stimulation, such as the xanthine derivatives, caffeine and theophylline, has shown some efficacy in published clinical trials" (Spec., p. 3, l. 10-12). While Pugliese suggests that the primary cause of cellulite is estrogen (Spec., p. 3, l. 12-13), nevertheless, "[c]ellulite is a condition seen only in women and is characterized by the formation of fatty deposits . . . in the thighs and the buttocks" (Spec., p. 4, l. 8-9). Thus, while Pugliese's specification does not explicitly define the term "cellulitis" in Claim 8, it appears from the art of record that "[c]ellulitis is ['an inflammatory condition of cellular or connective tissues' (AB12, footnote)] formed by local accumulation of fat" (Soudant, col. 1, l. 66-68); i.e., a medical condition relating to local accumulation of fat.

Soudant teaches the topical application or oral administration of multicomponent anticellulitic compositions including at least one lipolytic agent thought to erase local accumulation of fat for use

in combating cellulitis, eliminating local fat overload, and slimming (Soudant: cols. 1-2). Soudant's compositions may include one or more lipolytic agents selected from a group including xanthines and carnitine (Soudant, col. 2, l. 27-42).

Koulbanis teaches the topical application of multicomponent cosmetic compositions having slimming and anti-cellulitis action including at least one xanthine. Xanthines selected from theophylline, caffeine and theobromine are thought by Koulbanis to erase local accumulation of fat by increasing lipolytic action and thus be useful for treating skin with rolls of fat and cellulitis (Koulbanis, cols. 3, l. 47-51).

Sekiya teaches percutaneous (Sekiya, col. 2, l. 1-3 and 49 (application onto skin)) or oral administration of multicomponent compositions (Sekiya, col. 1, l. 55-59) including at least one isoflavone which is said to promote fat-degradation and weight reduction (Sekiya, cols. 1-2).

Majeed teaches topical or oral administration (Majeed, col. 4, l. 47-49) of compositions containing a forskohlin extract from the Coleus Forskohli plant and other nutritional supplements (Majeed, col. 2, l. 55-63) to promote lean body mass while simultaneously reducing body fat (Majeed, col. 1, l. 67, to col. 2, l. 6, and

col. 3, l. 37-53). Majeed states, "It is well known in the literature that forskohlin is related to lipolysis in isolated fat cells . . ." (Majeed, col. 2, l. 19-35). Suitable carriers, diluents and excipients for topical administration of forskohli are said to be well known in the art (Majeed, col. 4, l. 47-49).

Kuppusamy teaches that the flavonoids "quercetin and fisetin were potent PDE [phosphodiesterase] inhibitors which were also among the more active lipolytic compounds (Table 2). Fisetin was only half as potent, as a PDE inhibitor, when compared to quercetin but showed greater lipolytic activity than quercetin" (Kuppusamy, p. 1312, col. 2). See Kuppusamy's Table 2 (p. 1309) for the comparative PDE activity and lipolysis of other test compounds including theophylline, genistein, and daidzein. Moreover, fisetin and quercetin caused a synergistic increase in lipolysis in the presence of other drugs (Kuppusamy, p. 1313, col. 2, to p. 1314, col. 1). The prior art recognized that "[c]ompounds that cause direct lipolysis may have a use in anti-obesity therapy . . ." (Kuppusamy, p. 1307, col. 2).

Lotte (English translation of Japanese Patent Publication Hei 7-61927) teaches one or more (Lotte, p. 9) lipase-inhibiting agents for oral administration with foods and beverages to control digestion and absorption of lipids and control and prevent obesity

(Lotte, pp. 4, 6 and 13). An example of a preferred lipase-inhibiting agent is the flavonol quercetin (Lotte, p. 7).

De Simone teaches oral or topical administration (De Simone, (Claims 7, 9 and 10) of compositions including carnitine derivatives such as L-acetylcarnitine, L-isovalerylcarnitine and L-propionylcarnitine, and pharmaceutically acceptable salts thereof, to increase glucose uptake, reduce ketones and fatty acids, to increase protein synthesis (De Simone, p. 1, middle para.), and for therapeutic treatment of obesity and regeneration of cutaneous, intestinal, hepatic and other tissue (De Simone, pp. 1-2, bridging para.).

We find that each and every prior art reference cited by the examiner pertains to therapeutic compositions for oral and/or topical administration to control, prevent, reduce or relieve accumulation of fat. Thus, we find that all of the cited prior art references are analogous to the subject matter Pugliese claims.

We proceed to consider whether the combined teachings of the prior art prima facie would have led persons having ordinary skill in the art to make and use multicomponent compositions comprising (1) quercetin or fisetin, (2) genistein or daidzein, (3) an L-carnitine, (4) a xanthine such as theophylline, theophylline salt, caffeine, or theobromine, (5) Coleus Forskohli

plant extract, and (6) solubilizing and (7) emulsifying agents useful in formulating oil-in-water emulsions therewith for topical treatment of localized fat accumulation, cellulite and cellulitis associated therewith. The prior art need not explicitly direct the combination of each component of the composition with every other or every other combination of components. It is sufficient that the examiner concluded that persons having ordinary skill in the art reasonably would have expected success in treating localized fat accumulation, cellulite and/or resultant cellulitis using each one or subcombinations of previously disclosed active agents to establish that a combination of all the previously disclosed active agents prima facie would have been obvious for a common purpose. See In re Kerkhoven, 626 F.2d 846, 850, 205 USPQ 1069, 1072 (CCPA 1980):

> It is prima facie obvious to combine two compositions each of which is taught by the prior art to be useful for the same purpose, in order to form a third composition which is to be used for the very same purpose. . . . [T]he idea of combining them flows logically from their having been individually taught in the prior art.

Prima facie obviousness under 35 U.S.C. § 103 has been established in this case because the prior art teachings, considered as a whole, implicitly would have suggested Pugliese's claimed multicomponent composition and method for its use to persons having

ordinary skill in the art with reasonable expectation of success. See In re O'Farrell, 853 F.2d 894, 903, 7 USPQ2d 1673, 1681 (Fed. Cir. 1988)(for obviousness under § 103, all that is required is a reasonable expectation of success). Moreover, the examiner correctly states that it is not necessary for our holding of obviousness that persons having ordinary skill in the art would have been led to make and use the compositions and methods Pugliese claims for the reasons Pugliese discloses. See In re Dillon, 919 F.2d 688, 693, 16 USPQ2d 1897, 1901 (Fed. Cir. 1990)(en banc), cert. denied, 500 U.S. 904 (1991):

> Each situation must be considered on its own facts, but it is not necessary in order to establish a prima facie case of obviousness that . . . the claimed compound or composition will have the same or a similar utility.

On consideration of the prior art as a whole, we conclude that persons having ordinary skill in the art reasonably would have been led to make and use compositions comprising at least one of the components selected from (a) quercetin and fisetin, (b) genistein and daidzein, (c) carnitine, (d) theophylline, caffeine and theobromine, and (e) plant extract of Coleus Forskohli, with solubilizing and/or emulsifying agents suitable for oral or topical treatment of obesity, accummulation of fat, localized accumulation of fat, cellulite or associated cellulitis. Each of the prior art agents is said to be active for promoting fat degradation and/or

lean body mass, controlling digestion and absorption of lipids, increasing lipolysis, inhibiting phosphodiesterase activity, slimming, treating obesity, treating cellulite, treating cellulitis or regenerating tissue. Thus, it also would have been obvious to make and use the multicomponent compositions Pugliese claims for any of the reasons the applied prior art suggests with reasonable expectation that the compositions would generally promote fat degradation and/or lean body mass, control digestion and absorption of lipids, increase lipolysis, inhibit phosphodiesterase activity, promote slimming, treat obesity or regenerate tissue. Persons having ordinary skill in the art reasonably would have expected that compositions comprising all the active agents described by the applied prior art would promote fat degradation and/or lean body mass, control digestion and absorption of lipids, increase lipolysis, inhibit phosphodiesterase activity, cause slimming, treat obesity and regenerate tissue associated with cellulite and associated cellulitis.

Most of the cited references explicitly state that the agents described are thought to be active for treating localized accumulation of fat when administered orally or topically with suitable solubilizing and emulsifying agents for the elected form of delivery. See, for example, Soudant, col. 3, l. 49, col. 4, 64, and

Examples 1-8; Koulbanis, col. 2, l. 67, to col. 3, l. 54, and Examples III-VI; Majeed, col. 4, l. 47-49; and Sekiya, col. 2, l. 35-58.

There are more explicit reasons why persons having ordinary skill in the art would have combined agents thought to be active for promoting fat degradation and/or lean body mass, controlling digestion and absorption of lipids, increasing lipolysis, inhibiting phosphodiesterase activity, promoting slimming, treating obesity and regenerating tissue. First, certain of the cited prior art references expressly state that persons having ordinary skill in the art should combine active agents for a variety of reasons. Soudant teaches persons having ordinary skill in the art to combine lipolytic agents selected from a group including "growth factors . . . xanthines . . . [and] carnitine . . ." (Soudant, col. 2, l. 27-42). Soudant explains that certain slimming agents, for example, the phosphodiesterase-inhibiting xanthine, caffeine, cannot be used in high concentration (Soudant, col. 2, l. 15-24; emphasis added):

> [Caffeine,] particularly at high concentrations, is not always tolerated, even topically, because it penetrates and may give rise to palpitations in certain particularly sensitive. . . . [G]rowth factors are excellent substitutes or supplements for caffeine. . . . [I]t is assumed that growth factors owe their lipolytic effect to an action mechanism different from that of caffeine.

Koulbanis teaches persons having ordinary skill in the art to combine at least one xanthine derivative with compounds which stimulate the desirable activity by a different mechanism (Koulbanis, col. 2, l. 1-13). Koulbanis explains (Koulbanis, col. 1, l. 43, to col. 2, l. 6; emphasis added):

> [I]t is . . . important to inhibit the action of the phosphodiesterase in order to have a high level of cyclic AMP in the adipocytes with the aim of stimulating the lipolytic activity.
>
> Among the different phosphodiesterase inhibitors which have been proposed, there may be mentioned in particular the xanthic bases, and more particularly theophylline, caffeine and theobromine. However, it has been shown that the results obtained with these inhibitors, taken by themselves or in association with the abovementioned enzymes, is not very satisfactory with regard to reducing cellulitis.
>
> . . . . .
>
> We have now found, . . . that it is possible to act on the cellulitis and achieve a slimming action by using a cosmetic composition containing certain sulphur-containing compounds in association with certain substituted xanthines.
>
> . . . . .
>
> No explanation can currently be provided for the excellent activity observed. However, it is thought that these compositions may stimulate the activity of the cytochrome oxidases. In other words, these compositions may stimulate cellular respiration and oxidative metabolism.

Lotte teaches that "flavoids can be used alone or different kinds of them can be mixed together" (Lotte, p. 9, first full sentence). Kuppusamy teaches that "[m]any drugs used in the

treatment of various clinical disorders have been shown to exert a synergistic increase in lipolysis . . ." (Kuppusamy, p. 1313, col. 2, second para.). Poor solubility and resultant low concentrations may limit the lipolytic activity of a single active agent. Thus, higher total concentrations of active agents may be able to induce lipolysis not achievable using a single active agent. Id. Kuppusamy reports that the flavoids fisetin and quercetin, "potent PDE inhibitors that exerted a competitive mode of inhibition, showed a wide range of effects on lipolysis" (Kuppusamy, p. 1314, col. 1, first full para.).

Majeed teaches that it was "well known in the literature that forskohlin is related to lipolysis in isolated fat cells . . . (Majeed, col. 2, l. 19-20; emphasis added). Forskohlin is reported to be useful for the promotion of lean body mass (Majeed, col. 2, l. 34-35) and may be use in combination with other nutritional supplements (Majeed, col. 2, l. 61-63). Sekiya proposes the use of isoflavones such as daidzein and genistein to promote lipolysis since lipolytic agents such as caffeine and theophylline were reported to cause adverse effects (Sekiya, col. 1, l. 11-26). Persons having ordinary skill in the art would have known that PDE inhibition and lipolytic activity are agent/dose dependent. However, not all strong PDE inhibitors are strong lipolytic agents

and vice versa. See Kuppusamy, p. 1309, Table 2. Accordingly, it prima facie would have been obvious in view of either the implicit and explicit teachings of the applied prior art to combine two or more of the agents described by the applied prior art to promote fat degradation and/or lean body mass, control digestion and absorption of lipids, increase lipolysis, inhibit phosphodiesterase activity, cause slimming, treat obesity and regenerate tissue by the same or different mechanisms in amounts effective to promote that desired activity without undesirable side effects.

Having determined that a prima face case of obviousness has been established in view of the combined prior art teachings, we consider Pugliese's evidence of nonobviousness. Pugliese's primary evidence of nonobviousness is the Declaration of P.T. Pugliese under 37 C.F.R. §1.68 and 1.132, dated April 30, 2001, including attached Exhibits A, B and C (Paper No. 5). According to Dr. Pugliese, Formulas #1, #2 and #3 (Spec., pp. 10-12), each comprising the isoflavone genistein, were evaluated for efficacy in treating the cosmetic condition in women called cellulite according to the protocol indicated on page 12 of the specification entailing ultrasound measurements on thigh diameters (Paper No. 5, p. 1, para. 3-4). Pugliese's specification describes the Formula #1 Emulsion,

the Formula #2 Microencasulation and the Formula #3 Emulsion as comprising the following active components (Spec., pp. 10-11):

Formula #1 Emulsion

Fisetin	.001 to 5.0 wt.%	oil phase
Genistein	0.1 to 2 wt.%	oil phase
Theophylline acetate	.001 to 4.0 wt.%	water phase
Coleus forskohlii extract	.001 to 2.0 wt.%	water phase
L-carnitine	.001 to 2.0 wt.%	oil phase

Formula #2 Microencapsulation

Quercetin	.001 to 5.0 wt.%
Genistein	.001 to 5.0 wt.%
Theophylline acetate	.001 to 4.0 wt.%
Coleus forskohlii extract	.001 to 2.0 wt.%
L-carnitine	.001 to 1.5 wt.%

Formula #3 Emulsion

Quercetin	.001 to 5.0 wt.%	oil phase
Genistein	.001 to 5.0 wt.%	oil phase
Theophylline acetate	.001 to 4.0 wt.%	water phase
Coleus forskohlii extract	.001 to 2.0 wt.%	water phase
Acetyl L-carnitine	.001 to 1.5 wt.%	oil phase

Dr. Pugliese declares (Paper No. 5, para. 5-11):

> 5. Genistein was first evaluated for its potential effects on the fat reduction of female thighs, as to be determined by ultrasound measurements, which measurements are presented graphically in the tricolor bar charts depicted in Exhibit A, titled "Density Measurements of Ultrasound Scans";

> 6. Such measurements were made at 1 (blue bar), 28 (purple bar), and 56 (yellow bar) day intervals starting from initial topical application of Formula No. 3, assess average epidermis density, average papillary dermis density, and average reticular dermis density, respectively;

7. Papillary dermis density is an indicator of connective tissue cell replacement, while reticular dermis density is an indicator of reduction in fat cell size and/or number;

8. As a medically licensed physician and clinician, it is my professional opinion that the exemplary isoflavone, genistein, shows a measurable increase (c. 5 units) in epidermis density at 28 days, followed by a slight dip at day 56; a progressive increase in papillary dermis density from c. 27 units at day one to c. 48 units at day 56; and, a progressive increase in reticular dermis density from c. 35 units at day 1 to c. 66 units at day 56;

9. Five women with clinically determined moderate cellulite were treated with an emulsion like Formula #3, but having active components, save genistein being omitted, and the emulsifiers and emollients being retained, with twice daily applications to both thighs; the degree of cellulite was determined by measuring visual ratio of connective tissue to fat infiltration into connective tissue;

10. Based on ultrasound measurements, made at both four and eight weeks, the amount of fatty tissue decreased, while the amount of connective tissue increased by about 8% at four weeks, and by 19% at eight weeks, respectively (Exs. B & C).

11. From the foregoing graphic presentations of my clinical observations, I am able to conclude that genistein, in combination with afore-described active components, or even if used alone in an emulsion, is capable of inhibiting the undesirable destructive effects of estrogen on connective tissue, like collagen, and it thus provides a positive effect on treating cellulite, as indicated by measuring their visual ratios as recited above.

We have carefully considered Pugliese's declaration, especially the procedure, the visual observations, the objective results reported in the attached exhibits, and the conclusions Dr. Pugliese has drawn therefrom. We are somewhat confused by the lot.

Even if we presume to understand precisely what the components and component proportions of the formulations with and without genistein that Pugliese tested on the thighs of women exhibiting cellulite, precisely how the measurements were taken and recorded, and the individual and comparative reliability of the observations and data recorded for each formulation with and without genistein, Pugliese concludes at best that genistein alone, or genistein in combination with other known active agents, provides a positive effect on treating cellulite. Pugliese's declaration that the claimed subject matter is patentable is less persuasive and carries less weight than the combined teachings of the applied prior art that the claimed subject matter would have been obvious to persons having ordinary skill in the art for treating cellulite with reasonable expectation of success. Kuppusamy shows that genistein is an excellent PDE (phosphodiesterase) inhibitor with at least four times the PDE inhibition potency as alternative isoflavone daidzein (Kuppusamy, p. 1309, Table 2). Sekiya teaches that the isoflavones genistein and daidzein promote degradation of fat when percutaneously administered (Sekiya, col. 1, l. 55, to col. 2, l. 62). Soudant and Koulbanis teach that PDE inhibition is the key to combating cellulitis and PDE inhibitors can be effectively administered topically (Soudant, col. 1, l. 58, to col. 2, l. 24;

Koulbanis, col. 1, l. 34, to col. 3, l. 54). "Expected beneficial results are evidence of obviousness of a claimed invention, just as unexpected beneficial results art evidence of unobviousness." In re Skoll, 523 F.2d 1392, 1397, 187 USPQ 481, 484 (CCPA 1975). Here, the prior art cited by the examiner would have led persons having ordinary skill in the art reasonably to expect at least the beneficial results Pugliese reports. Declarations that reported results are unexpected must be supported by evidence. Assertions and conclusory statements that results are unexpected cannot themselves establish patentability, especially where the prior art reasonably would have led persons having ordinary skill in the art to expect all that Pugliese's objective evidence of unobviousness shows.

Moreover, genistein is not representative of all the alternative isoflavones of Pugliese's claims. Note that genistein is four times the PDE inhibitor than its alternative daidzein is (Kuppusamy, p. 1309, Table 2). Accordingly, Pugliese showing is not commensurate in scope with the scope of the compositions and methods claimed. "[O]bjective evidence of nonobviousness must be commensurate in scope with the claims." In re Kulling, 897 F.2d 1147, 1149, 14 USPQ2d 1056, 1058 (Fed. Cir. 1990).

We have considered all the evidence and arguments favoring patentability and all the evidence and arguments to the contrary. In our view, the examiner's case for unpatentability of the claimed subject matter under 35 U.S.C. § 103 is supported by the greater weight of all the evidence. Accordingly, we affirm the examiner's final rejection of Claims 1-7 and 9-11 of Application 09/989,019 under 35 U.S.C. § 103 in view of the combined teachings of Soudant, Koulbanis, Majeed, Sekiya, De Simone, Lotte, Kuppusamy, and Gennaro. AFFIRMED.

New Ground of Rejection Under 37 CFR § 41.50(b)

THIS IS A NEW GROUND OF REJECTION. Method Claim 8 of Application 09/989,019 is hereby rejected anew under 35 U.S.C. § 103 in view of the combined teachings of Soudant, Koulbanis, Majeed, Sekiya, De Simone, Lotte, Kuppusamy, and Gennaro. In the Examiner's Answer (Paper No. 11), the examiner withdrew this rejection upon reconsideration. However, the examiner's reasons why the rejection of Claim 8 was withdrawn are unclear. In the paragraph bridging pages 3-4 (EA3-4), the examiner indicated that the cited prior art, save Koulbanis and Soudant, are silent on treating cellulites. We disagree. As we have indicated hereinabove, Kuppusamy shows that genistein, quercetin, and fisetin are potent PDE (phosphodiesterase) inhibitors (Kuppusamy, p. 1309,

Table 2). Sekiya teaches that the isoflavone genistein promotes degradation of fat when percutaneously administered (Sekiya, col. 1, l. 55, to col. 2, l. 62). Soudant and Koulbanis teach that PDE inhibition is the key to combating cellulitis and that anti-cellulitis PDE inhibitors can be effectively administered topically (Soudant, col. 1, l. 58, to col. 2, l. 24; Koulbanis, col. 1, l. 34, to col. 3, l. 54). Accordingly, the combined prior art, considered as a whole, would have reasonably taught persons having ordinary skill in the art that oil-in-water emulsions comprising tolerable amounts of one or more known PDE inhibitors and one or more agents active in promoting lipolysis and/or lean body mass and/or tissue regeneration by various mechanisms reasonably could be expected to effectively treat localized fat accumulation in women, cellulite and cellulitis associated therewith and arising therefrom. We conclude that the method of Claim 8 of Application 09/989,019 would have been prima facie obvious under 35 U.S.C. § 103 to a person having ordinary skill in the art in view of the combined prior art teachings. The compositions for use in the method of Claim 8 are unpatentable under 35 U.S.C. § 103 in view of the same prior art teachings for treatment of localized fat accululation, cellulite, and associated cellulitis.

37 CFR § 41.50(b).

Conclusion

For the reasons stated herein, it is ORDERED that:

the examiner's final rejection of Claims 1-7 and 9-11 of Application 09/989,019 is affirmed; and

as a NEW GROUND OF REJECTION UNDER 37 CFR § 41.50(b),

Claim 8 of Application 09/989,019 is rejected under 35 U.S.C. § 103 in view of the combined teachings of Soudant, Koulbanis, Majeed, Sekiya, De Simone, Lotte, Kuppusamy, and Gennaro of record in this appeal.

This decision contains a new ground of rejection pursuant to 37 CFR § 41.50(b) (effective September 13, 2004, 69 Fed. Reg. 49960 (August 12, 2004), 1286 Off. Gaz. Pat. Office 21 (September 7, 2004)). 37 CFR § 41.50(b) provides "[a] new ground of rejection pursuant to this paragraph shall not be considered final for judicial review."

37 CFR § 41.50(b) also provides that the appellant, WITHIN TWO MONTHS FROM THE DATE OF THE DECISION, must exercise one of the following two options with respect to the new ground of rejection to avoid termination of the appeal as to the rejected claims:

> (1) *Reopen prosecution*. Submit an appropriate amendment of the claims so rejected or new evidence relating to the claims so rejected, or both, and have the matter reconsidered by the examiner, in which event the proceeding will be remanded to the examiner. . . .
>
> (2) *Request rehearing*. Request that the proceeding be reheard under § 41.52 by the Board upon the same record. . . .

No time period for taking any subsequent action in connection with this appeal may be extended under 37 CFR § 1.136(a)(1)(iv).

AFFIRMED; 37 CFR § 41.50(b)

TEDDY S. GRON)
Administrative Patent Judge)
)
)
DONALD E. ADAMS) BOARD OF PATENT
Administrative Patent Judge) APPEALS
) AND
) INTERFERENCES
)
DEMETRA J. MILLS)
Administrative Patent Judge)

TG/dym

Appeal No. 2005-0545
Application No. 09/989,019

TG/dym

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